



Serial No. 10/826,112
Atty. Docket No.: P71641US0

IN THE UNITED STATES PATENT AND TRADEMARK OFFICE

In re the Application of:

Reuben MATALON

Group Art Unit: 1609

Serial No.: 10/826,112

Examiner: Meghan R. Finn

Filed: April 17, 2004

For: METHODS AND MATERIALS FOR TREATING CONDITIONS ASSOCIATED WITH
METABOLIC DISORDERS

DECLARATION OF Jan Ruud Hansen

Commissioner of Patents
P.O. Box 1450
Alexandria, VA 22313-1450

Sir:

I, Jan Ruud Hansen, do hereby declare the following:

1. I reside at Galschioetsvej 12, DK 3000 HELSINGOER, Denmark.
2. My educational background and professional experience is set forth on my Curriculum Vitae (CV) attached hereto as Attachment A. As indicated, I have over 20 years experience in statistical data analysis and quality control. As a result of my education and experience, my professional contemporaries

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and colleagues consider me an expert in the above mentioned fields.

3. Based upon my education and experience, I have an opinion regarding what the level of ordinary skill in the metabolic disorder treatment field generally would be. Persons of ordinary skill in this art would include those individuals having attained a Bachelor or Master of Science degree in medicine, chemistry, physiology, biology or biotechnology or at least five years of experience in developing nutritional supplement products.
4. Drawing upon my expertise, I understand the level of ordinary skill in the art at the time the above-captioned application was originally filed (July 2003), and can offer my expert opinion as to how persons of ordinary skill in the art would perceive and respond to relevant art in the field of metabolic disorders and nutritional treatment thereof.
5. I have read and understand the application identified in the caption and the proceedings in connection therewith, including the Final Office Action of August 1, 2008.

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6. The Examiner has rejected claims 17-36 as being anticipated by Wachtel et al. (DE 4037447 A1) (Wachtel). According to the Examiner, Wachtel teaches an amino acid composition consisting of Histidine, Isoleucine, Valine, Threonine, Methionine, Leucine, Tryptophan, Tyrosine and Lysine and teaches weight ratios, which the Examiner calculates to be within the claimed ranges of Applicant and therefore anticipated by Wachtel.

7. Applicant's representative has previously stated that Wachtel, when translated from German, states, "the weight ratios may vary with $\pm 10\%$ and $\pm 20\%$, respectively, of the mentioned values." It is Applicant's understanding that when the weight% in Wachtel is given as, for example, $14.5 \pm 10\%$, this does not mean that the weight% of the substance varies from 4.5 to 24.5 weight%. What is meant in Wachtel is that the weight% value itself may vary by 10%, or between about 13.05 to about 15.95 weight%. Applicant's representative also remarked in the previous Response, that it did not appear to make scientific sense to consider the deviations of $\pm 10\%$ and $\pm 20\%$ to mean weight%, because if the values of the actual weight% were below 10 or 20, one would arrive at a

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zero, or negative value, for the amino acid component of the proposed diet.

8. I have read the Examiner's Response to Applicant's arguments in the present Final Office Action dated 08/01/2008. The Examiner responds by stating that the Applicants interpretation of the deviations figures is one, but not the only possible interpretation of the art (Office Action at page 3). The Examiner further responds by stating that one of ordinary skill in the art would have understood that the percentage values could not be less than zero, so that zero would be understood to be the minimum value in the stated range (Office Action at page 4). The Examiner goes on to make the statement that "the mere fact that the +/- 20% range can lead to negative values is not reason enough to assume that the 10% value is only in relation to the percentage claimed. I respectfully disagree with these statements.

9. I have read and understand Wachtel. In my expert opinion, one of ordinary skill in the art would understand that the percentage deviation (+/- %) in the table in Claim 4 of Wachtel is a percentage deviation of the unit given in the

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table header, which is weight%. A +/-20 % deviation of 5.0 weight% gives a range of 4.0 - 6.0 weight%. Similarly, a +/-20 % deviation of 5.0 mg gives a range of 4.0 - 6.0 mg. In my expert opinion, this is the only possible interpretation of the percentage deviation (+/- %) in the table in Claim 4 of Wachtel. There are no indications in Wachtel that the deviations should or could be understood as a percentage of the total. On page 11 (of the English translation) Wachtel states that "the proportions of lysine, isoleucine, leucine, valine and tyrosine can deviate by up to +/- 10 % and for the remaining amino acids by up to +/- 20 % of the mentioned value". The units for the proportions are in weight% and the units for the deviations are % of the weight% value. The table on page 10 mentions a weight% value of 14.5 for the proportion of lysine. As 10 % of 14.5 equals 1.45, and the unit for the mentioned value is weight%, Wachtel teaches that proportion of lysine can vary in the range 13.05 - 15.95 weight% depending on the individual metabolism situation. The values presented in Wachtel are relative quantities of amino acids added to a diet, or a recipe. One of ordinary skill, when following the teaching of Wachtel, would understand what the approximate weight% of each ingredient or

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amino acid should be in proportion to the total amount in the diet. The values in the table are not the result of an experimental determination of a value. The amounts of added amino acid component shown are under direct control of the person making the diet. An analogy can be made to a recipe for a cake. One would not expect a recipe for a cake which called for 4 cups of flour +/- 20% to mean 4 cups of flour +/- 20 cups of flour.

10. Furthermore, in my professional experience, if one were to prepare a composition which included a number of ingredients, it would not make sense, to one of ordinary skill in the art, to disclose an amount of 5 weight% +/- 20% to mean that the amount of compound added to the composition could vary from 0 to 25 weight%, when one could have just as easily stated the range as 0 - 25 weight%, or, in the alternative, stated the range as (12.5 +/- 12.5) weight%, and therefore not state a negative range.
11. The Examiner defends her interpretation of the deviation percentages as being weight-percentages, by arguing that it is standard practice in the art of giving totals that equal more

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than 100%. I disagree with the Examiner's analogy. It is my expert opinion that examples that the Examiner are referring to are generally understood by those of skill in the art to be due to "rounding errors" introduced when percentages of individual component values are rounded to the next whole percent. In that situation, if one of skill were to add the various component percentages, one could arrive at a sum with a number greater than 100%. This is not the case in Wachtel. The values stated are the proportion of amino acids added in the diet recipe, and there is no teaching regarding the rounding of the percentage values. On page 11 (of the English translation) Wachtel states that "If one (or many) amino acids is used in a large quantity, then, it is obvious that one (or many) other amino acids is used in a smaller proportion". Based on the above statement one of ordinary skill in the art would appreciate that the total obviously must be 100 weight%.

12. I further declare that all statements made herein of my own knowledge are true and that all statements made on information and belief are believed to be true; and further that these statements were made with the knowledge that willful false

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statements and the like so made are punishable by fine or imprisonment or both, under section 1001 of Title 18 of the United States Code; and that such willful false statements may jeopardize the validity of the application or any patent issuing thereon.

01-21-2008

January 21, 2008

Date

A handwritten signature in black ink, appearing to read 'Jan Ruud Hansen', with a stylized, flowing script.

Jan Ruud Hansen

Attachment A: CV of Jan Ruud Hansen

CURRICULUM VITAE

Jan Ruud Hansen
Galschiotsvej 12
DK-3000 HELSINGØR
Denmark

Telephone: +45 4576 2616 (private)
 +45 3079 9226 (mobile)
 +45 5138 7501 (work)

Day of birth: 01 June 1956

Education

- 1981 "Høgskolekandidat" in software engineering,
Agder University College, Kristiansand, Norway.
- 1976 Military Police (national service training),
The Norwegian Navy Military Police School, Bergen, Norway.
- 1975 High school diploma in economics, Sandefjord Handelsgymnas,
Sandefjord, Norway.

Current employment

SAS Institute A/S,
Købmagergade 7-9
DK-1150 København K

Position: Chief Consultant.

Statistical analysis of labor market data for the Danish government.

Statistical Quality Control in Danish Healthcare.

Employment

2004 – 2005 NNE A/S, Gladsaxevej 372, 2860 Søborg, Denmark

Position: Consultant.

Writing strategies for process analytical technology (PAT) tools (analyzers, measurement systems, data analysis software). Novo Nordisk A/S (2004-2005).

Risk assessment of hardware platform upgrade of a SAP R3 ERP system used for management of regulatory records. Ferrosan A/S (2004).

Review of the quality system in a medical device manufacturing organization. Ferrosan A/S (2004).

Development, validation and implementation of a spectroscopic method for identity test of active pharmaceutical ingredients. Novo Nordisk A/S (2005).

Feasibility study for developing a PAT ready process for a pharmaceutical raw material supplier. Name withheld under secrecy agreement, Sweden (2005)

Participating in the definition and writing of the PAT strategy for a finished pharmaceuticals organization. Novo Nordisk A/S (2005).

Process review and data analysis of process and quality data for finished pharmaceuticals manufacturing sites. Novo Nordisk A/S (2005).

Identification of improvement opportunities and initiation of improvement projects for finished pharmaceuticals manufacturing sites. Novo Nordisk A/S (2005).

LEAN and Six Sigma implementation in a medical device manufacturing organization. Ferrosan A/S (2005).

Coaching NNE consultants in statistical data analysis, statistical quality control and process analytical technologies.

2000 – 2004 HiQ Wise A/S, IT and Management Consultant.

Software and database design, development and validation as consultant to Foss Electric A/S (2000) and to NNE A/S (2000 - 2004).

As consultant to NNE A/S:

- Development and validation of a Windows security and COM+ based authentication and authorization system enabling manufacturing execution systems and process control system to comply with electronic records and electronic signatures regulations from the US Food and Drug

Administration and the European Agency for the Evaluation of Medicinal Products.

- Development and validation of manufacturing execution system modules.
- Assessment and evaluation of regulatory compliance of computer systems with respect to current good manufacturing practices and other regulations from the US Food and Drug Administration and the European Agency for the Evaluation of Medicinal Products (e.g. electronic records and electronic signatures). Defining and implementing remediation strategies for noncompliant systems. The systems ranged from laboratory instrument control and data acquisition systems to ERP systems (SAP R3). Novo Nordisk A/S (2003-2004). Ferrosan A/S (2004)
- Statistical data analysis of process- and laboratory data (using SAS software). Novo Nordisk A/S (2003-2004). Ferrosan A/S (2004)
- Development, validation and implementation of a spectroscopic method for quantitative determination of water content in an active pharmaceutical ingredient. Novo Nordisk A/S (2004).

1999 Scandinavian School of Brewing, teaching Statistical Quality Control

1997 – 2000 Carlsberg Corporate Operations Control, Carlsberg A/S, Project manager

Responsible for the design, development and implementation of a Quality Control and Laboratory Information System for all Carlsberg associated breweries worldwide. System rollout and training of personnel at more than 30 breweries. Design development and implementation of an executive quality information system for Carlsberg Corporate Operations Control and Carlsberg executive presidents.

1987 – 1997 Carlsberg Research Center, Carlsberg A/S, Project manager and senior data analyst

Statistical analysis of data from brewing related research projects and brewing processes. Design and Implementation of research oriented software applications. Project manager for the IT project "IT infrastructure at Carlsberg Research Center". Project manager for the R&D project "Acquisition and statistical analysis of brewing process data"

1984 – 1987 Center for Experimental Design and Data Processing, Norwegian Agricultural Research Council, Chief software engineer

Local area networks and integration of PC's with the central mainframe. PC support for employees and students at The Agricultural University of Norway. Teaching "Personal computer hardware and software", "Applied statistics" and "Statistical software (SAS and SYSTAT)". Project manager for two "Laboratory Information Management System" projects.

1981 – 1984 The Norwegian Directorate for Nature Management, Fish Research Division, Software engineer and data

Responsible for design and implementation of IT systems for registration and statistical data analysis of fish tagging experiments. Design of the Norwegian Hunters database. Studies on migration activity of salmonids and silver eels.

1980 – 1981 Agder University College, Kristiansand, Norway. Assistant teacher (part time job)

Teaching in "Microcomputer technology" and "Computers and Society".

1976 – 1977 Supreme Headquarters Allied Powers Europe, Belgium. Military police (national service)

Courses

2004 - LabVantage Sapphire LIMS, NNIT A/S, Copenhagen

2003 - Project management, Connector, Copenhagen

2001 - GMP, Software Validation, FDA 21 CFR Part 11, NNE A/S, Copenhagen

1995 - Project management, SYNTAX, Copenhagen

1990 - Accessing databases with The SAS System, SAS, Paris.
- Diploma in quality management, DIEU, Copenhagen

1989 - Statistical Quality Control, SAS, Cologne.

1988 - VAX/VMS System maintenance II, DEC, Copenhagen
- Presentation techniques, OT Management, Copenhagen

1987 - VAX/VMS Performance and capacity planning, Raxco, Basel
- VAX/VMS System maintenance I, DEC, Copenhagen
- Quantitative Chemometrics, ØIH/NR, Sarpsborg, Norway

1984 - VM/SP Installation workshop, IBM, Oslo.

1983 - Statistical methods, The Agricultural University of Norway, Ås

Special competences

- SAS software
- Executive information systems
- Explorative data analysis
- Statistical quality control
- Six Sigma
- Software development life cycle
- Software validation
- FDA 21 CFR Part 11, Electronic Records; Electronic Signatures
- FDA 21 CFR Part 820, Quality Systems
- FDA 21 CFR Part 211, Current Good Manufacturing Practices
- Process analytical technology (PAT)
- Good manufacturing practice for the 21st Century (FDA initiative)

Congresses, presentations

Participated in and made presentations at several meetings, symposia and congresses.

Languages

Scandinavian, English

Hobbies

Fly fishing, mountaineering, judo, skiing and golf

PUBLICATIONS AND PRESENTATIONS

1. Jonsson, B and J. Ruud-Hansen (1985). Water temperature as the Primary Influence on Timing of Seaward Migrations of Atlantic Salmon (*Salmo salar*) Smolts. *Can.J.Fish.Aquat.Sci.* 42: 593-595
2. Vøllestad, L.A., B. Jonsson, N.A.Hvidsten, T.F. Næsje, Ø Haraldstad and J.Ruud-Hansen(1986). Environmental factors regulating the seaward migration of European silver eels (*Anguilla anguilla*). *Can.J.Fish.Aquat.Sci.* 43: 1909-1916
- 3 Ruud-Hansen, J., T. Kaasen and A. Jørgensen (1987). The PC SAS System in a Laboratory Environment. *Proceedings SEUGI'87*, 503-509
- 4 Jonsson, N., B. Jonsson and J. Ruud-Hansen (1988). Downstream displacement and life-history traits of whitefish, *Coregonus lavaretus*, in a Norwegian river. *Env.Biology of Fishes* 23, 197-204
- 5 Ruud-Hansen, J. (1988). SAS Systemet i et VAX/PC miljø. *SUGS'88 Oslo* (also presented at SUGD, DECUS Denmark and DECUS Iceland)
- 6 Jonsson, B., N. Jonsson and J. Ruud-Hansen (1989), Downstream Displacement and Life History Variables of Arctic Charr (*Salvelinus alpinus*) in a Norwegian River. *Jap.Journal of Physiology and Ecology*, Spec. volume 1, 1989, 93-105
- 7 Francisco, Alicia de, J. Ruud-Hansen and Lars Munck (1989). Correlation between visual assessment of pre-harvest sprouting of wheat and the alpha-amylase content of grain and flours, In: *Wheat is Unique*, ed. Y.Pomeranz, AACC, 1989
- 8 Munck. L., K.G.Jørgensen, J.Ruud-Hansen and K.T.Hansen (1989). The EBC-methods for Determination of High Molecular Weight B-Glucan in Barley, Malt, Wort and Beer. *Monatsschrift für Brauwissenschaft*, 1989, 162-166
- 9 Aastrup, S., P.Riis and J.Ruud-Hansen (1989). High vigour - the basis for high malting barley quality. *Proceedings EBC Congress 1989*, 171-178
- 10 Riis, P, S.Aastrup and J.Ruud-Hansen (1989). Controlled, rapid and safe removal of dormancy in malting barley. *Proceedings EBC Congress 1989*, 195-202
- 11 Mouritsen, S., M.Meldal, J.Ruud-Hansen and O.Werdølin (1991). T-Helper-Cell Determinants in Protein Antigens are Preferentially Located in Cysteine-Rich Antigen Segments Resistant to Proteolytic Cleavage by Cathepsin B, L and D. *Scand.J.Immunol.*34, 1991

- 12 Ruud-Hansen, J. (1991). Implementing a Quality System using SAS Software. Proceedings SUGS'1991 Oslo.
- 13 Leah, R., K.Skriver, S.Knudsen, J.Ruud-Hansen, N.V.Raikhei and J.Mundy(1994). Identification of an enhancer/silencer sequence directing the aleurone-specific expression of a barley chitinase gene. The Plant Journal (1994) 6(4), 579-589
- 14 Ruud-Hansen, J. (1997). En subklasse af Data Table..... SUGD'97 Copenhagen.
- 15 Ruud-Hansen, J. (1997). Erfaringer med kvalitetsstyring vha SAS. SUGD'97 Copenhagen.
- 16 Skands, B., P.Riis, H.Thomsen and J.Ruud-Hansen (1997), Studies of yeast behavior in fully automated test plant. Proceedings EBC Congress 1997, 413-421
- 17 Ruud-Hansen, J. (1997). Search and Research into Migration Patterns and Reproduction Strategies of Anguilla spp. (Eel). Carlsberg Laboratory Christmas Dinner 1997.
- 18 Ruud-Hansen, J. (1998). Quality Management within Carlsberg. SUGS'98 Stockholm (invited)
- 19 Ruud-Hansen, J. (2000). Hvorfor anvende SAS systemet ved kvalitetsstyring i produktion. SUGD'2000 Copenhagen
- 20 Heinze, C.L. and J. Ruud Hansen (2005). Implementing PAT Step by Step as a Process Optimization Tool. Pharmaceutical Engineering May/June 2005, Volume 25, Number 3, 8-16